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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/368,076	08/03/1999	HONG JIN	7682-047	5091

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PENNIE & EDMONDS LLP
1667 K STREET NW
WASHINGTON, DC 20006

EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/368,076

Applicant(s)

JIN ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-39 and 42-50 is/are pending in the application.
- 4a) Of the above claim(s) 36-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

1. Claims 36-39 and 42-50 are pending in the application. Claims 36-39 stand withdrawn as to non-elected inventions. Claims 42-50 are under consideration.
2. Previously pending claims 40-44 were rejected in the prior action mailed on June 18, 2003. In the Response filed on October 20, 2003, the Applicant amended claims 42 and 44, and added new claims 45-50.
3. Because this action raises grounds of rejection art raised in the prior action, this Office action is being made Non-Final.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. **(New Rejection)** Claims 42, 43, and 45-49 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. These claims read on isolated RSV particles with truncations of the M2-1 gene, such that a stop codon is inserted at one of a series of positions listed (e.g.) in claim 43. With the exception of the stop codons at positions 8137-8139, and 8140-8142 (representing a deletion of either 17 or 16 amino residues respectively), the Applicant has not shown adequate operability such that the Applicant is entitled to RSV particles comprising the M2-1 truncations identified in (e.g.) claim 43.

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As noted by the Applicant, the truncation at the amino residue encoded by the codon of nucleotide positions 8137-39 represents a 17-residue truncation of the M2-1 protein. The art teaches that truncations of the M2-1 protein longer than 17 residues do not result in viable RSV particles. See, Tang et al. (J Virol 75: 11328-35, at 11330. In particular, the reference specifically teaches that truncations of 46 and 67 residues (which appear to coincide with the truncations at the first four positions identified in claim 43) failed to result in viable RSV particles. Thus, because the claims read on RSV particles disclosed by the art to be inoperable, the claims are rejected as lacking utility.

6. **(New Rejection)** Claims 45-49 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. These claims read on RSV particles with substitutions of the M2-1 Cys3His motif. I.e., due to the inclusion of claim 49, which further limits claim 45 to embodiments wherein the motif is retained, the claims implicitly indicate that RSV particles lacking this motif are included in claim 45. However, the art teaches that no viable viruses could be obtained when the codons encoding for the residues of this motif were mutated. See, Tang et al. (supra, abstract and page 11330, teaching that, although multiple attempts were made, no virus containing mutations within this motif could be obtained). Because the art teaches that viruses with substitutions within the Cys3His motif are not operable, the Applicant has not demonstrated a sufficient utility to support the claims to such RSV particles.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Withdrawn)** Claims 40 and 41 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated infectious RSV comprising a substitution of a glycine for cysteine residue 96, does not reasonably provide enablement for an isolated RSV wherein any cysteine residue has been substituted. These claims have been cancelled from the Application. In view of the cancellation, the rejection of these claims is withdrawn.

9. **(Prior Rejection-Restated and Maintained)** Claims 42 and 43 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a deletion mutant of M2-1 wherein the truncation is at amino residues 178 or 179 (nucleic acids 8137-8139 or 8140-8142 respectively), does not reasonably provide enablement for any viable truncated M2-1 protein. In particular, the claims have been rejected as lacking enablement for the deletion mutants of M2-1 wherein truncations are inserted at codon positions other than 8137-8139, or 8140-8142. For the purposes of this rejection, new claim 48 is read as though it depended from claim 47. In view of the addition of new claims 47 and 48, which add the limitations of claims 42 and 43 to claim 45, the rejection of these claims is extended to claims 45-49. Thus, claims 42, 43, and 45-49 are rejected under 35 USA 112, first paragraph for the reasons indicated in the prior action, and the reasons indicated below.

The Applicant traverses the rejection on the basis that those in the art would be capable of performing the required assays to determine whether the other claimed embodiments result in

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operative embodiments (i.e. there is no undue experimentation required to distinguish between operative and inoperative embodiments).

In addition to the uncertainty in the present application regarding the viability of the RSV particle with M2-1 deletion mutant, the Examiner is also not persuaded by Applicant's traversal due to the teachings by Tang et al., J Virol 75(23): 11328-35. This reference teaches that attempts to develop the presently claimed attenuated RSV have failed, with the exception of the deletion mutant of claim 50, to produce viable RSV particles. Tang, abstract, and page 1330, second full paragraph. Because the art teaches that viable RSV particle may not be obtained when the M2-1 gene comprises a C-terminal deletion of over 17 residues, the Applicant is not enabled for any attenuated RSV particles comprising deletions longer than 17 residues. Thus, in view of these teachings, it is irrelevant whether those in the art could easily determine if these truncations would result in attenuated virus because the art teaches that such truncations are inoperative. For this reason, and for the reasons of record, the rejection of claims 42 and 43 as lacking enablement are maintained.

10. **(Prior Rejection- Maintained)** Claim 44 was rejected in the prior action under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contained subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. That claims has been amended to add new functional language to the claim such that the claim needs to read on viruses with "a lower degree of virulence as compared to the wild type virus." In view of the amendments to this claim, the rejection is withdrawn.

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However, newly added claim 45 has been drafted such that it comprises the language of the previously rejected claim 44, except that it makes no mention at all of the residues of the cysteine motif in the N-terminal end of the protein (cysteines 7, 15, and 21, and histidine 25), and includes the new functional language. New claim 49 has been also been added to the application, which claim explicitly requires that the motif is retained in the RSV particle of claim 45, thereby impliedly indicating that claim 45 reads on embodiments where the motif is not maintained. The rejection is therefore withdrawn as to claim 44, but extended to and maintained over new claims 45-48.

The Applicant has argued in the Response that those in the art would be able to easily determine (i.e. without undue experimentation) what other mutations in combination with the substitution at residue 96 would result in a viable RSV particle according to the claims. Thus, it appears that the Applicant is attempting to rely on this functional language to avoid the prior rejection based on the teachings in the art that the Cys₃-His zinc-binding motif is required for M2-1 protein function. See, Hardy, page 5884, and U.S. Patent 6,376,171, column 2, lines 31-45 (cited in prior action, teaching that conservation of the Cys₃-His motif is required for protein function, and not that only serine substitutions destroy that functionality). However, for examination purposes, claims are given their broadest reasonable interpretation. By inclusion of claim 49 in the claim set, the Applicant has provided a basis for one of ordinary skill in the art to reasonably infer that claim 45 (from which claim 49 depends) reads on RSV wherein substitutions have been made in the Cys₃His motif. This is because claim 49, as dependant to claim 45, should be further limiting of that claim. Thus, because claim 49 explicitly limits the

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particles of claim 45 to embodiments wherein the motif is retained, claim 45 must implicitly include such embodiments.

Because the claims must be read such that claims 45 and its dependant claim 47 read on embodiment comprising a mutation in the Cys₃-His motif, the claims are found as lacking enablement. In addition to the teachings referred to above, indicating that the motif is required for M2-1 function and that the M2-1 protein is required for viral viability, additional teachings in the art further indicate that the RSV particles claimed by the applicant are inoperative. In particular, an article by Tang et al. (J Virol 75: 11328-35) specifically teaches that substitution of any of the residues of the Cys₃His motif results in an inability to recover viable RSV particles. See, abstract, and page 11334 (page 11334 explicitly stating that the results disclosed in the article support the teachings of Hardy). Thus, the art clearly indicates that the Applicant is not enabled for any substitution in the Cys₃His motif. For this reason, and for the reasons of record, the rejection is maintained, and extended to claims 45-48.

11. **(Prior Rejection- Withdrawn)** Claim 44 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Prior to amendment, this claim read on isolated attenuated RSV with "at least one M2-1 mutation, wherein at least one gene mutation encodes an amino exchange from a cysteine to an amino acid selected from the groups comprising glycine,

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valine, aspartic acid, and alanine at amino acid position 96...” In view of the amendments to claim 44, the rejection is withdrawn as to this claim.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. **(Prior Rejection-Withdrawn)** Claim 44 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendments made to the claim, the indefiniteness rejections of this claim are withdrawn.

14. **(New Rejection-Necessitated by Amendment)** Claims 42-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on an attenuated RSV particle that “exhibits a lower degree of virulence compared to a wild type virus.” It is not clear from the claims what comprises “a wild type virus.” For example, it is unclear if the term refers to any virus, to any respiratory syncytial virus, or a virus of the type from which the attenuated virus was derived.

15. **(New Rejection-Necessitated by Amendment)** Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 48 recites the

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limitation "wherein the stop codon causing said C-terminal truncation ..." There is insufficient antecedent basis for this limitation in the claim. Neither of the claims from which claim 48 depends, either directly or indirectly, identifies a stop codon causing a C-terminal truncation. Thus, because it is not clear from claim 48 what stop codon, or what C-terminal truncation, the claim is referring to, the claim is rejected as indefinite.

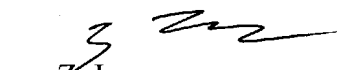
Conclusion


16. No Claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner


JAMES HOUSEL 1/24/04
SUPERVISORY PATENT EXAMINER
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